RESPONSE

I. Rejection of Claims 1-3, 13 and 14 Under 35 U.S.C. § 101

The Action continues to reject claims 1-3, 13 and 14 under 35 U.S.C. § 101 for the reasons already of record on pages 3-6 of the Office Action dated September 10, 2002. Applicants in turn persist in their traverse.

The Action disagrees with Applicants' logical assertion, based on the evidence, that the sequences of the present invention encode a novel human transporter protein. Applicants disagree, as the presently claimed sequence is clearly referred to as a transporter protein (see, at least, the title and specification Section 2), and the sequence are clearly identified as transporter proteins that share structural similarity with mammalian sugar and sodium-dependent inorganic phosphate transporters. In addition the application identifies transporter proteins as integral membrane proteins that mediate or facilitate the passage of materials across the lipid bilayer and identifies the role of transporter proteins in the export of chemotherapeutics and thus their role in multiple drug resistance. Thus, the biological role of the presently claimed transporter protein is well defined, it facilitates the transport of materials, more specifically sugar and inorganic phosphates, across the lipid bilayer.

Further evidence of the role of the sequences of the present invention as transporter protein is provided in the form of protein functional domain analyses using several methods known and accepted by those of skill in the art. **Exhibit A** is a compilation of the results of functional protein domain analyses using several of the available methods known to and accepted by those of skill in the art.

InterPro (http://www.ebi.ac.uk/interpro/) is a database of protein families, domains and functional sites in which identifiable features found in known proteins can be applied to unknown protein sequences. InterPro analysis of SEQ ID NO:2 of the present invention clearly shows it to be, as Applicants have asserted, a transporter protein.

Pfam (http://www.sanger.ac.uk/Software/Pfam/index.shtml) is a large collection of multiple sequence alignments and hidden Markov models covering many common protein domains and families. For each family in Pfam you can: Look at multiple alignments; View protein domain architectures; Examine species distribution; Follow links to other databases; View known protein structures. Pfam analysis of SEQ ID NO:2 of the present invention once again clearly shows it to be, as Applicants have

asserted, a transporter protein.

ProtComp analysis (http://www.hgmp.mrc.ac.uk/GenomeWeb/prot-anal.html)is used in Identifying sub-cellular location of a protein in animals and fungi. Results of a ProtComp analysis of SEQ ID NO:2 of the present invention shows it to be an integral membrane protein. Applicants have asserted that the sequences of the present invention encode a transporter protein, which those of skill in the art would recognize to be an integral membrane protein.

SMART (a Simple Modular Architecture Research Tool: http://smart.embl-heidelberg.de/) analysis allows the identification and annotation of genetically mobile domains and the analysis of domain architectures. More than 500 domain families found in signaling, extracellular and chromatin-associated proteins are detectable. These domains are extensively annotated with respect to phyletic distributions, functional class, tertiary structures and functionally important residues. Each domain found in a non-redundant protein database as well as search parameters and taxonomic information are stored in a relational database system. User interfaces to this database allow searches for proteins containing specific combinations of domains in defined taxa. SMART analysis of SEQ ID NO:2 of the present invention once again clearly shows it to be, as Applicants have asserted, a transporter protein.

TMHMM analysis (http://www.cbs.dtu.dk/services/TMHMM/) predicts transmembrane helices in proteins and TMHMM analysis of SEQ ID NO:2 of the present invention once again clearly shows it to be an integral transmembrane protein, as those of skill in the art would expect of a transporter protein.

Finally, ProDom analysis (http://prodes.toulouse.inra.fr/prodom/2002.1/html/home.php) is a comprehensive set of protein domain families automatically generated from the SWISS-PROT and TrEMBL sequence databases. ProDom analysis of SEQ ID NO:2 of the present invention once again clearly shows it to be, as Applicants have asserted, a transporter protein.

In summary, the evidence presented as a result of analysis using a series of methods recognized by those of skill in the art, clearly identify the sequences of the present invention as encoding an integral membrane transporter protein, as Applicants have asserted. Therefore, Applicants assertion that the sequences of the present invention encode a transporter protein are clearly credible and would be accepted by those of skill in the art.

Given the historic legal test for utility simply involves an assessment of whether those skilled in

the art would find any of the utilities described for the invention to be credible or believable, this is clear evidence that those skilled in the art would have recognized the function and activity of the protein encoded by the sequences of the present invention, there can, therefore, be no question that Applicants' asserted utility for the described sequences is "credible." According to the Examination Guidelines for the Utility Requirement, if the applicant has asserted that the claimed invention is useful for any particular purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 Federal Register 1098, January 5, 2001).

The Action discounts Applicants' assertion regarding the use of the presently claimed polynucleotides on DNA chips, based on the position that such a use would allegedly be generic. Applicants disagree and believe that as set forth in Applicants previous responses, given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. The claimed sequence provides a specific marker of the human genome (see evidence below), and that such specific markers are targets for discovering drugs that are associated with human disease. Thus, those skilled in the art would instantly recognize that the present nucleotide sequence would be an ideal, novel candidate for assessing gene expression using, for example, DNA chips, as the specification details. Further evidence of utility of the presently claimed polynucleotide, although only one is needed to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), is the utility the present nucleotide sequence has a specific utility in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions, as described in the specification and evidenced below. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences (see evidence below). In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10

megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Only a minor percentage of the genome actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed, spliced, and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Equally significant is that the claimed polynucleotide sequence defines how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The Applicants respectfully submit that the practical scientific value of expressed, spliced, and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. For further evidence in support of the Applicants' position, the Examiner is requested to consider the evidence provided in Applicants' previous Response. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome as described in many articles.

As still further evidence supporting Applicants assertions of the specific utility of the sequences of the present invention in localizing the specific region of the human chromosome and identification of functionally active intron/exon splice junctions is the information provided in **Exhibit B**. This is the result of a blast analysis using SEQ ID NO:1 of the present invention when compared to the identified human genomic sequence. This result indicates that the sequence of the present invention is encoded by 13 exons spread non-contiguously along a region of human chromosome 20, more specifically 20q at approximately 62.25-62.4M bp, which are contained within clone AL121673.41. Thus clearly one would not simply be able to identify the13 protein encoding exons that make up the sequence of the present intention from within the large genomic sequence. Nor, would one be able to map the protein encoding regions identified specifically by the sequences of the present invention without knowing exactly what those specific sequences were.

Finally, the Examiner has determined that applicants argument of due process presented in previous response is not persuasive. Applicants understanding is that issued United States patents

retain a legal presumption of validity which in this case indicates that the inventions claimed in the cited patents are *legally presumed* to be in full compliance with the provisions of 35 U.S.C. sections 101, 102, 103, and 112. Applicants respectfully submit that, absent a change in the law as enacted by Congress and signed by the President, it is improper for the Examiner to hold Applicants' invention to a different legal standard of patentability. Given the rapid pace of development in the biotechnology arts, it is difficult for the Applicants to understand how an invention fully disclosed and free of prior art at the time the present application was filed, could somehow retain *less* utility and be *less* enabled than inventions in the cited issued U.S. patents (which were filed during a time when the level of skill in the art was clearly lower). Simply put, Applicants invention is *more* enabled and retains *at least as much* utility as the inventions described in the claims of the U.S. patents of record. Any argument to the contrary is at best arbitrary and at worst capricious. Absent authority provided by an act of Congress or Executive order, arbitrary or capricious conduct by an administrative office the U.S. government has historically proven to conflict with the provisions of the U.S. Constitution. The Patent Office does not have the authority to rewrite U.S. law. However, the Patent Office does have a Constitutional obligation to administer U.S. law in an unbiased and procedurally consistent manner. That is what the Applicants are respectfully requesting the Examiner to consider in the present matter. As the issued U.S. Patents cited above are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph, Applicants respectfully submit that the presently claimed polynucleotide must also meet the requirements of 35 U.S.C. § 101.

For each of the foregoing reasons, Applicants submit that in light of the above discussion and those presented in previous Applicant responses, the presently claimed invention has been shown to have a substantial, specific, credible and well-established utility and that the rejection of pending claims 1-3,13 and 14 under 35 U.S.C. § 101 has been avoided, and respectfully request that the rejection be withdrawn.

II. Rejection of Claims 1-3, 13 and 14 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-3, 13 and 14 under 35 U.S.C. § 112, first paragraph for reasons already of record page 6 of the Office action dated September 10, 2002 as well as for the reasons given in the above rejection under 35 U.S.C. § 101. Applicants respectfully traverse and

submit that as claims 1-3, 13 and 14 have been shown to have "a specific, substantial, and credible utility", as detailed in section IV above, and therefore respectfully request withdrawal of the rejection of claims 1-3, 13 and 14 under 35 U.S.C. § 112, first paragraph.

III. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Landsman have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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